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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/983,025	10/22/2001	Claus Oxvig	OXVIG=1A	7756

7590 02/10/2004

BROWDY AND NEIMARK, P.L.L.C.
624 Ninth Street, N.W.
Washington, DC 20001

EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/983,025	OXVIG ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-19,30-47,49-53,55-59,62 and 70-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-19 and 70-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Claims 12-19, 30-47, 49-53, 55-59, 62, 70-89 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's amendment of claims 12-17, 30, 56-58, addition of claims 70-89, cancellation of claims 1-11, 20-29, 48, 54, 60-61, 63-69, and election with traverse of Group II, claims 12-19, drawn to the polypeptide of SEQ ID NO: 2, in a communication filed on 11/24/2003 are acknowledged.

Applicant's traverse is on the ground(s) that Groups VII, IX, X, XIV, XV and XVIII are properly rejoined with Group II pursuant to MPEP 821.04 provided that a claim of Group II is allowable. Applicant's arguments have been fully considered but are not deemed persuasive to withdraw the restriction requirement. It is noted that non-elected claims 53 and 59 are directed to different products and not to processes. With regard to process claims, in accordance with the provisions of MPEP § 821.04, the Examiner will rejoin withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Claims 30-47, 49-53, 55-59, 62 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Newly added claims 70-89 are directed to the elected invention, i.e. the polypeptide of SEQ ID NO: 2, and are being examined in the instant application.

Specification

1. In response to a statement made by the previous Examiner of record regarding a specific reference in the first sentence of the specification for receiving benefit of an earlier filing date, Applicants assert that an amendment to the specification was filed on 10/22/2001 to indicate a priority claim to provisional application No. 60/241,840 filed on 10/20/2000. As indicated by Applicants, page 2 of the transmittal letter contains such amendment.

Priority

2. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/241,840 filed on 10/20/2000.

3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to DENMARK PA 2000 01571 filed on 10/20/2000.

4. It is noted that the polypeptide of SEQ ID NO: 2 was first disclosed on 10/20/2000 (provisional application No. 60/241,840 and DENMARK PA 2000 01571).

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on 3/11/2002, 9/3/2002, and 9/27/2002 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Drawings

6. The drawings filed on 10/22/2001 are accepted by the Examiner.

Claim Objections

7. Claims 13-17 are objected to due to the recitation of "PAPP-A2". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. It is suggested that the term "pregnancy associated plasma protein A2" be recited at least once. Appropriate correction is required.

8. Claims 13-19 are objected to due to the following informalities: for clarity, it is suggested that the term "the" be inserted prior to the recitation of "polypeptide according". Appropriate correction is required.

9. Claim 19 is objected to due to the recitation of "proteins natively associated with said polypeptide". For clarity, it is suggested that the term be amended to recite "proteins naturally associated with said polypeptide". Appropriate correction is required.

10. Claims 71-75 are objected to due to the recitation of "polypeptide of claim X comprising an…". For clarity, it is suggested that the term be replaced with "polypeptide of claim X wherein said polypeptide comprises…". Appropriate correction is required.

11. Claims 76-82, 84 are objected to due to the recitation of "in which ..reference sequence". For clarity, it is suggested that the term be replaced with "wherein the reference …". Appropriate correction is required.

12. Claims 76-82 are objected to due to the recitation of "AAs". Abbreviations unless otherwise obvious and/or commonly used in the art, should not be recited in the claims without at least once reciting the entire phrase for which the abbreviation is used. It is suggested that the term "amino acids" be recited at least once. Appropriate correction is required.

13. Claims 83, 85-89 are objected to due to the recitation of "polypeptide of claim X which....". For clarity, it is suggested that the term be replaced with "polypeptide of claim X wherein said polypeptide...". Appropriate correction is required.

14. Claim 84 is objected to due to the recitation of "reference sequence is amino acids 234 to 1791 of SEQ ID NO: 2". For clarity, it is suggested that the term be amended to recite "reference sequence consists of amino acids...". Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 12-19 and 70-89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

17. Claim 12 (claims 13-19 and 70-89 dependent thereon) is indefinite in the recitation of "polypeptide comprising an amino acid sequence having at least....., or a fragment thereof, wherein said polypeptide, and, if said reference sequence is a fragment, said fragment, i) has proteolytic activity..., ii) is recognized by an antibody..., and/or iii) competes with a polypeptide...for binding to a cell surface receptor with an affinity for said polypeptide" for the following reasons. As written, one cannot determine if the term "fragment thereof" refers to a fragment of the amino acid sequence of SEQ ID NO: 2 or if it refers to a fragment of the claimed polypeptide. The terms "fragment thereof" and "if said reference sequence is a fragment" appear to imply that the term "fragment thereof" refers to a sequence fragment which is used as a reference to determine the % identity. As such, one could interpret the term "having at least 75% sequence identity with a reference sequence which is SEQ ID NO: 2, or a fragment thereof" as meaning "75% sequence identity to the entire sequence of SEQ ID NO: 2 or a 75% sequence

identity to a fragment of the sequence of SEQ ID NO: 2". Thus, the characteristics recited in i), ii) and iii) can apply only to the polypeptide claimed and not to the "fragment" of SEQ ID NO: 2 used as a reference to determine % identity. In addition, it is noted that, as known in the art, a sequence is a graphical representation of the order in which nucleotides/amino acids are arranged in a molecule. Consequently, the amino acid sequence fragment recited in the claim cannot have functional characteristics associated with polypeptides or polypeptide fragments. The term "competes with a polypeptide...for binding to a cell surface receptor with an affinity for said polypeptide" is unclear and confusing since one cannot determine which polypeptide is referred to by the term "said polypeptide", the claimed polypeptide or the polypeptide of SEQ ID NO: 2. For examination purposes, it will be assumed that the claim is directed to an isolated polypeptide or a fragment thereof, wherein said polypeptide comprises an amino acid sequence having at least 75% sequence identity with a reference sequence, wherein said reference sequence is SEQ ID NO: 2 or a fragment of SEQ ID NO: 2, wherein said polypeptide or fragment thereof, i) has proteolytic activity...., ii) is recognized by an antibody..., and/or iii) competes with a polypeptide having the amino acid sequence of SEQ ID NO: 2 for binding to a cell surface receptor, wherein said cell surface receptor has affinity for the polypeptide having the amino acid sequence of SEQ ID NO: 2. Correction is required.

18. Claim 13 is indefinite in the recitation of "the reference sequence is...., corresponding to the mature part of ....., including any processing variant thereof" for the following reasons. The term "including any processing variant thereof" is unclear since one cannot determine if it is further limiting the claim or how it further limits the claim. In addition, the term "processing variant" is unclear as one cannot determine its meaning and the specification fails to provide a definition for this term. For examination purposes, no patentable weight will be given to the term. Correction is required.

19. Claim 18 is indefinite in the recitation of "polypeptide according to claim 12, wherein said polypeptide is a recombinant polypeptide" since the term "recombinant polypeptide" does not further

limits the claim. It is unclear as to which are the physical/chemical characteristics in a "recombinant polypeptide" which are different from the "isolated polypeptide" recited in claim 12, from which claim 18 depends. If the intended limitation is in regard to how the polypeptide is made, the claim should be amended accordingly. For examination purposes, it will be assumed that the claim is drawn to the polypeptide of claim 12, wherein said polypeptide is produced recombinantly. Correction is required.

20. Claim 77 is indefinite in the recitation of "in which the reference sequence comprises AAs 234 to 1791 of SEQ ID NO: 2" as it is unclear how it further limits claim 70. Claim 70 is directed to a polypeptide having the amino acid sequence of SEQ ID NO: 2. As such, a limitation regarding the reference sequence is irrelevant since the claimed polypeptide is 100% sequence identical to the polypeptide of SEQ ID NO: 2. For examination purposes, it will be assumed that claim 77 is a duplicate of claim 70. Correction is required.

21. When amending the claims, Applicants are advised to carefully review all examined claims and make the necessary changes to ensure proper antecedent basis and dependency.

Claim Rejections - 35 USC § 112, First Paragraph

22. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

23. Claims 12-16, 18-19, 71-84, and 88-89 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 12-16, 18-19, 71-84, and 88-89 are directed to a genus of polypeptides of <u>any</u> function, wherein said polypeptides comprise (1) an amino acid sequence which has at least 75%-98% sequence

identity with the amino acid sequence of SEQ ID NO: 2, (2) an amino acid sequence which has at least 75%-98% sequence identity with fragments of the amino acid sequence of SEQ ID NO: 2, (3) the amino acid sequence of (1) or (2) wherein said amino acid sequence also has at least 7 or 17 contiguous amino acids of a fragment of SEQ ID NO: 2, wherein said fragment consists of amino acids 234-1791 of SEQ ID NO: 2. See Claim Rejections under 35 USC 112, second paragraph for claim interpretation.

While the specification discloses the structure and function of the polypeptide of SEQ ID NO: 2, the specification is completely silent regarding the functions or structures of all the polypeptides encompassed by the claims. The genus of polypeptides claimed is an extremely large variable genus encompassing polypeptides of diverse functions. As taught by the art, a high degree of structural homology may not result in functional homology. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) teaches that polypeptides of approximately 67% homology to a desaturase from *Arabidopsis* were found to be hydroxylases once tested for activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Broun et al. (Science 282:1315-1317, 1998) teaches that as few as four amino acid substitutions can convert an oleate 12-desaturase into a hydrolase and as few as six amino acid substitutions can transform a hydrolase to a desaturase. Therefore, as taught by the art, a genus of polypeptides sharing structural homology have the potentiality of encoding proteins of many different functions.

In addition, while a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the

genus, in the instant case, the recited structural features, such as "75%-98% sequence identity to a fragment of the amino acid of SEQ ID NO: 2" or "at least 7 or 17 contiguous amino acids of a fragment of SEQ ID NO: 2 consisting of residues 234-1791", do not constitute a substantial portion of the genus as the remainder of any polypeptide comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected. Many functionally and structurally unrelated polypeptides are encompassed by these claims. The specification only discloses a single species of the claimed genus which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

24. Claims 12-16, 18-19, 71-84, and 88-89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, (2) a polypeptide comprising residues 234-1791 of the polypeptide of SEQ ID NO: 2, and (3) fragments of (1), does not reasonably provide enablement for polypeptides of any function wherein said polypeptides comprise (a) an amino acid sequence which has at least 75%-98% sequence identity with the amino acid sequence of SEQ ID NO: 2, (b) an amino acid sequence which has at least 75%-98% sequence identity with fragments of the amino acid sequence of SEQ ID NO: 2, (c) the amino acid sequence of (a) or (b) wherein said amino acid sequence also has at least 7 or 17 contiguous amino acids of a fragment of SEQ ID NO: 2, wherein said fragment consists of amino acids 234-1791 of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3)

the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims as described above is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides of unknown function encompassed by the claims. As indicated above, the specification discloses the function and structure of the polypeptide of SEQ ID NO: 2. However it does not provide any information as to the structures or functions of all the polypeptides encompassed by the claims. Furthermore, the specification does not provide any information as to the critical structural elements required in any polypeptide to encode a pregnancy associated plasma protein A2 (PAPP-A2) nor does it provide any information as to (1) which amino acids of the polypeptide of SEQ ID NO: 2 are essential for the only function disclosed, i.e. PAPP-A2, or (2) which amino acids in the polypeptide of SEQ ID NO: 2 can be modified (i.e. substituted, inserted or deleted) to create a structural homolog as recited in the claims with PAPP-A2 activity.

The state of the art teaches the unpredictability of determining function using structural homology and discloses examples of how small structural changes can lead to major changes in function. See the teachings of Broun et al., Van de Loo et al., Seffernick et al., and Witkowski et al. already discussed. Since structure determines function, one of skill in the art would require some knowledge or guidance as to how structure correlates with PAPP-A2 function. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display PAPP-A2 activity, the lack of knowledge about other functions encompassed by claims, and the unpredictability of the prior art in regard to function based on homology, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) screen and isolate those polypeptides, as encompassed by the claims, having PAPP-A2 function, and (2) determine the actual function of those claimed polypeptides which do not have PAPP-A2 function. Thus, Applicant has not

provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claims 12-13, 18-19, 71-76, 78-84, 88-89 are rejected under 35 U.S.C. 102(a) as being anticipated by Farr et al. (Biochim. Biophys. Acta, 1493:356-362, October 2, 2000; cited in the IDS; SPTREMBL accession number Q9H4C9).

Claims 12-13, 18-19 and 76 are directed in part to polypeptides comprising an amino acid sequence having at least 75% sequence identity with SEQ ID NO: 2 or 75% sequence identity with a fragment of SEQ ID NO: 2 comprising residues 234-1791, wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2. Claims 71-75, 78-82 and 84 are directed in part to polypeptides comprising an amino acid sequence having at least 80%-98% sequence identity with a fragment of SEQ ID NO: 2 comprising/consisting of residues 234-1791, wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2. Claim 83 is directed in part to polypeptides comprising an amino acid sequence having at least 75% sequence identity with a fragment of SEQ ID NO: 2 wherein the amino acid sequence differs from that of the fragment of SEQ ID NO: 2 by one or more conservative substitutions, and wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2. Claims 88-89 are

directed in part to polypeptides comprising an amino acid sequence having at least 75% sequence identity with SEQ ID NO: 2 or 75% sequence identity with a fragment of SEQ ID NO: 2 comprising residues 234-1791, wherein said amino acid sequence comprises at least 7 or 17 contiguous amino acids of a fragment of the polypeptide of SEQ ID NO: 2 having residues 234-1791, and wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2. Farr et al. teaches a PAPP-E (pregnancy associated plasma protein E) having 1624 amino acids. The polypeptide of Farr et al. is 99.8% sequence identical to amino acids 168-1791 of the polypeptide of SEQ ID NO: 2 (4 mismatches; 99.8% = 1620x100/1624; see attached alignment) and contains one conservative mismatch at position 1739 of SEQ ID NO: 2. Since the polypeptide of SEQ ID NO: 2 and the polypeptide of Farr et al. share a substantial number of possible epitopes, they will also share antibodies which will react with both polypeptides. Therefore, the polypeptide of Farr et al. anticipates the claims as written.

26. Claims 12, 18-19, 71-75, 83, 88-89 are rejected under 35 U.S.C. 102(b) as being anticipated by Haaning et al. (PIR accession number S65464, November 1996).

Claims 12, 18-19, 71-75 are directed in part to polypeptides comprising an amino acid sequence having at least 75%-98% sequence identity with any fragment of SEQ ID NO: 2, wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2. Claim 83 is directed in part to polypeptides comprising an amino acid sequence having at least 75% sequence identity with any fragment of SEQ ID NO: 2, wherein the amino acid sequence differs from that of the fragment of SEQ ID NO: 2 by one or more conservative substitutions, and wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2. Claims 88-89 are directed in part to polypeptides comprising an amino acid sequence having at least 75% sequence identity with a fragment of SEQ ID NO: 2, wherein said amino acid sequence comprises at least 7 or 17 contiguous amino acids of a fragment of the polypeptide of SEQ ID NO: 2 having residues 234-1791,

and wherein said polypeptides are recognized by an antibody which reacts with the polypeptide of SEQ ID NO: 2.

Haaning et al. teaches a PAPP-A protein having 1627 amino acids. The polypeptide of Haaning et al. comprises several fragments which are 100% identical to fragments of the polypeptide of SEQ ID NO: 2. See attached alignment. All of the fragments of the polypeptide of SEQ ID NO: 2 comprised by the polypeptide of Haaning et al. correspond to fragments within amino acids 249-1790 of the polypeptide of SEQ ID NO: 2. The polypeptide of Haaning et al. also comprises at least 7 or 17 consecutive amino acids of the fragment of the polypeptide of SEQ ID NO: 2 consisting of amino acids 234-1791. See, for example, amino acids 818-835 of SEQ ID NO: 2. In addition, the polypeptide of Haaning et al. comprises several fragments which are at least 75% sequence identical to fragments of the polypeptide of SEQ ID NO: 2 and the mismatches between the fragments of the polypeptide of SEQ ID NO: 2 and the polypeptide of SEQ ID NO: 2 are conservative substitutions. See, for example, amino acids 1745-1759 of SEQ ID NO: 2. Since the polypeptide of SEQ ID NO: 2 and the polypeptide of Haaning et al. share a substantial number of possible epitopes, they will also share antibodies which will react with both polypeptides. Therefore, the polypeptide of Haaning et al. anticipates the claims as written.

Double Patenting

27. Applicant is advised that should claim 13 be found allowable, claim 76 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Relevant Art

28. Gu et a. (U.S. Patent No. 6656700, issued on 12/2/2003) teaches a PAPP-E protein which is 1770 amino acids long and is 99.9%. sequence identical to amino acids 1-1734 of the polypeptide of SEQ ID NO: 2 (2 mismatches). See attached alignment.

29. Page et al. (Placenta 22:681-687, 2001; cited in the IDS) teaches an alternative splice variant of a PAPP-E protein which is 1790 amino acids long and is 99.8% sequence identical to amino acids 2-1791 of the polypeptide of SEQ ID NO: 2 (3 mismatches). See attached alignment.

Conclusion

30. No claim is in condition for allowance.

31. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
February 4, 2004

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600